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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/978,464	10/16/2001	Frank L. Graham	ADVEC10IA-C1	5099
29847	7590	10/21/2003	EXAMINER	
VAN DYKE & ASSOCIATES, P.A. 7200 LAKE ELLENOR DRIVE, SUITE 252 ORLANDO, FL 32809			VOGEL, NANCY T	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/978,464	GRAHAM ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Nancy Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 02 September 2003.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 29 and 30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-28 and 31-34 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
     If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
     a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

### DETAILED ACTION

Claims 1-34 are pending in the instant case. Receipt of applicant's response received 9/2/03 is acknowledged. It is noted that although applicants state in their response that they wish to cancel non-elected claims 29 and 30, they did not do so in a formal amendment to the claims. This should be done in the next response.

#### ***Election/Restrictions***

Claims 29 and 30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 0903, submitted 9/2/03.

#### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-28 and 31-34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,379,943. Although the conflicting claims are not identical, they are not patentably distinct from each other because they contain limitations which overlap, or the claims recite overlapping groups of plasmids, or other specific nucleic acid sequences. Further, the plasmids or nucleic acid sequences are used for the same purpose: construction of infectious adenovirus vectors. The claims of the prior US patent recite a method for making an infectious adenovirus which comprises a first nucleic acid sequence encoding adenovirus sequences which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus and a second nucleic acid sequence which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus, each containing a site-specific recombinase recognition target site. The present claims differ in that they require head to head ITR junctions. Although not specifically claimed in the prior US patent, the claims of the prior patent embrace the instant claims because they provide for the efficient and reliable isolation of viral vectors using recombinase pathways. The methods of the prior patent embrace the instant claims because plasmids used in the prior patent do contain head to head ITRs such that the instant claims are an obvious variation on the prior claims.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 9, 14, 17, 18, 24, 25, 28, 30, 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the plasmids recited in these claims are required to practice the claimed inventions. Thus, these must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the plasmids. Although the Applicants describe the construction of the plasmids in the Figures, it is not clear that all of the nucleic acid sequences from which the plasmids were constructed are readily available to the public, and thus the plasmids of the claims may not be obtainable without deposit.

Where the invention involves a biological material and words alone cannot sufficiently describe how to make and use the invention in a reproducible manner, access to the biological material may be necessary for the satisfaction of the statutory requirements for patentability under 35 USC 112. Courts have recognized the necessity and desirability of permitting an applicant for a patent to supplement the written disclosure in an application with a deposit of biological material which is essential to

meet some requirement of the statute with respect to the claimed invention. *Merck and Col., Inc. v. Chase Chemical Co.*, 273 F. Supp. 68, 155 USPQ 139 (D. N.J. 1967); *In re Argoudelis*, 434 F.2d 666, 168 USPQ 99 (CCPA 1970).

Applicant claims various plasmid constructs in the instant claims. In order to sufficiently enable the claimed plasmids. Applicant must make a biological deposit of each of them. The deposit rules pursuant to 37 CFR 1.801-1.809 set forth examining procedures and conditions of deposit which must be satisfied when a deposit is required. See MPEP 2402-2404.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-23, 33 and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3, 10, 16, 33, and 34 recite the terms "insufficient" and "sufficient". These terms are relative in nature, which render the claims indefinite. These terms are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 13 is vague and indefinite as to the metes and bounds of the claim because it recites an expression cassette "derived from" a plasmid and a viral DNA

“derived from” a plasmid. “Derived” is a term that is non-specific and relative in nature for which Applicant provides no definition. It provides no clarity as to what Applicant’s claimed invention includes and what it does not include. Without a more specific definition, it is impossible to determine what and how many derivations comprise the invention. The nature and number of the derivations to arrive at the invention Applicant seeks to protect with the patent are not established such that a person skilled in the art would be apprised of the metes and bounds of the claims. The limits of the inventions cannot be discerned and others could not know if they were infringing Applicant’s claim.

Claims 9, 11, 18, 25, 28 and 31 are vague and indefinite in the recitation of “which, as optionally needed, undergo additional modification to provide a head-to-head ITR junction”. It is not clear from this phrase whether it is intended that the head-to-head ITR junction is present, or not, since it is not clear when such modification is “needed”. It is noted that rejected claims are indirectly dependent on claim 1, which recites that each of the first and second nucleic acid sequences comprise a head-to-head ITR junction. Furthermore, it is not clear how or when the recited modification takes place.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 10, 13, 16, 20, 33, 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Kaleko (WO 97/25446).

The invention of the instant claims is drawn to a method of generating infectious adenovirus which comprises a first nucleic acid sequence encoding adenovirus sequences which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus and a second nucleic acid sequence which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus. Each of the vectors in the present invention comprise a head to head inverted terminal repeat (ITR) and a recombinase recognition site.

Kaleko teaches a method for generating adenoviral vectors infectious adenovirus using recombinase-mediated transfer. See pages 5-9. The method uses a first polynucleotide including a heterologous DNA to be expressed, one or more adenoviral inverted terminal repeat (ITR), and adenoviral packaging signal and a recombinase target site. The second polynucleotide includes an adenoviral ITR. The second polynucleotide can also be a helper virus in which the adenoviral terminal protein is attached to the ITR. See page 12. As shown in Figures 7, 10, 19, and 24, the helper virus can contain two ITRs. Although the DL327lox sequence in the figures is shown as linear, it is interpreted that the ITRs are in a head-to-head orientation. If the sequence had been depicted as a circle, it is presumably drawn in a linear fashion because the terminal proteins are attached. See also pages 26-27. Adenoviral proteins for replication and packaging can be on the first polynucleotide, the second polynucleotide,



a third polynucleotide provided by the cell, or any combination thereof. The packaging signal can be deleted from the adenoviral sequences. See pages 12-13.

Claims 1, 2, 10, 12, 13, 16, 20, 33, 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Bett et al. (Proc. Natl. Acad. Sci. USA 91:8802-8806 (1994)).

The invention of the instant claims is drawn to a method of generating infectious adenovirus which comprises a first nucleic acid sequence encoding adenovirus sequences which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus and a second nucleic acid sequence which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus. Each of the vectors in the present invention comprise a head to head inverted terminal repeat (ITR) and a recombinase recognition site.

Bett et al. (1994) teach construction of an infectious adenovirus vector by the recombination of two sequences. As shown in Figure 3, one of the sequences, a pBGH plasmid, contains a head-to-head ITR junction indicated by the two arrows at the top of the plasmid. There is sufficient overlapping sequence for homologous recombination between the sequences when cotransfected into a cell such that the limitation of the present claims requiring sufficient overlap in the sequences for the purposes of recombination is met. The cells used are 293 cells and as such, they express E1 function. See notes on 293 in the instant specification on page 2, lines 4-5. See Fig. 3 of Bett et al.

Claims 1, 2, 10, 12, 13, 16, 19, 20, 33, 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Bett et al. (J. Virology 67:5911-5921 (1993)).

The invention of the instant claims is drawn to a method of generating infectious adenovirus which comprises a first nucleic acid sequence encoding adenovirus sequences which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus and a second nucleic acid sequence which in the absence of intermolecular recombination are insufficient to encode an infectious, replicable or packageable virus. Each of the vectors in the present invention comprise a head to head inverted terminal repeat (ITR) and a recombinase recognition site.

Bett et al. (1993) teach the construction of infectious adenovirus vectors by recombination between two nucleic acid sequences. In Figure 3 of the reference, a recombination between plasmid pFG173 and a pAB plasmid produces the infectious virus. Both pFG173 and the pAB plasmid contain head-to-head ITR junctions, as interpreted from the "110/0 mu" notation above each plasmid, which represents locations on the adenovirus vector where the ITRs reside. Figure 9b of the instant specification teaches a pAB vector that contains a foreign DNA insert and pFG173, and both are drawn with the two arrows at the top of the plasmid designating the head-to-head ITR junction. In the reference, the pAB vector is shown as having a deletion in E1 (see the topmost plasmid in the figure). The plasmids are cotransfected into 293 cells, which express E1 (see above rejection over Bett, 1994).

**Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy Vogel whose telephone number is (703) 308-4548. The examiner can normally be reached on 7:30 - 4:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ntv  
10/8/03

  
JAMES KETTER  
PRIMARY EXAMINER